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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,542	05/16/2001	Rajesh Manchanda	BERLX-100	9728

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EXAMINER	
WELLS, LAUREN Q	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,542	MANCHANDA, RAJESH	
	Examiner	Art Unit	
	Lauren Q Wells	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14,16-22 and 32-34* is/are pending in the application.

4a) Of the above claim(s) *7 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6, 8-14, 16, 18-22, 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-14, 16-22, 32-34 are pending. Claims 7, 17, are withdrawn from consideration, as they are directed to non-elected subject matter. The Amendment filed 5/10/04, amended claims 1, 7-8, 11, 17, and 31, and cancelled claims 23-25, 27-31, and 35.

Response to Applicant's Arguments/Amendment

The Applicant's arguments filed 5/10/04 to the rejection of claims 1-4, 6-14, 16-25, 27-35 made by the Examiner under 35 USC 103 have been fully considered and deemed not persuasive.

The Amendment to the claims filed 5/10/04, are sufficient to overcome the 35 USC 112 and 102 rejections in the previous Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 10-14, 16, 20-22, 33, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (6,174,513) in view of Banerjee et al. (2002/0151598).

The instant invention is directed toward a composition comprising a radionuclide, iodide ions or a compound which releases/generates iodide ions, and a targeting agent selected from a peptide, oligonucleotide, antibody, peptidomimetic, or the formula of instant claim 1, and method of stabilizing a composition comprising adding the iodide ions or a compound which releases/generates iodide ions to a composition comprising the radionuclide and targeting agent.

Miller et al. teach stabilization of peptides and proteins for radiopharmaceutical use, wherein surfactants in combination with salts are used to stabilize the peptides or proteins. Technetium-99m and others are taught as suitable radionuclides. The radiolabeled peptide is used with a pharmaceutically acceptable carrier in a method of performing a diagnostic imaging procedure in humans, wherein at least one tissue is targeted, using a scintillation camera. Saline is taught as a pharmaceutically acceptable carrier. The reference lacks compounds that generate/release iodine ions. See Col. 2, lines 11-22; Col. 3, lines 8-Col. 4, line 59; Col. 8, lines 9-42.

Banerjee et al. teach that tonicity adjusting agent can be added to saline solution to provide the desired ionic strength of the pharmaceutical composition. Potassium and sodium iodide are taught as tonicity adjusting agents which display no or only negligible pharmacological activity after in vivo administration. See [0056].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the potassium iodide, taught by Banerjee et al., to the saline solution of Miller et al. because of the expectation of achieving a composition wherein the tonicity can be adjusted to provide high, medium, or low ionic strength without effecting the pharmacological activity of the active agent.

While "a method of stabilizing a composition" is not explicitly stated, the Examiner respectfully points out that the above rejection teaches adding a compound which releases iodide ions to a composition comprising a radionuclide and a targeting agent. Thus, since the same steps are taught for affecting the composition, the method of the above rejection must have the property of stabilizing the composition.

Claims 8-9, 18-19, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Banerjee et al. as applied to claims 1-4, 6, 10-14, 16, 20-22, 33 and 34 above, and further in view of Blum et al. (Chest).

Miller et al. and Banerjee et al. are applied as discussed above. The reference lacks depreotide.

Blum et al. teach 99mTC depreotide as a somatostatin analog as an optimal imaging agent in scintiography for solitary pulmonary nodes. This compound is taught as having a great sensitivity for diagnosing malignant or benign pulmonary tumors. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the protein of the combined references as depreotide, as taught by Blum et al., because of the expectation of achieving an imaging agent that is highly sensitive in diagnosing the malignancy of pulmonary tumors and which does not undergo radiolysis (chemical decomposition of the peptide).

Response to Arguments

Applicant argues, regarding Bannerjee, "The filing dates of both of these applications are after applicants' filing date of May 16,2001. . .Although this provisional filing date is before applicants' filing date, the record does not indicate what the provisional application discloses". This argument is not persuasive. The Examiner has reviewed the provisional application upon which Bannerjee claims priority, and has found that the provisional application provides support for the disclosure of US 2002/0151598. The Applicant is more than welcome to do their own review of the abandoned provisional application per the Patent Office's rules for the public reviewing abandoned applications.

Applicant argues, "Bannerjee teaches nothing at all regarding stabilizing radiolabeled peptides or proteins or anything even remotely related thereto". This argument is not persuasive. The Examiner respectfully points out that the motivation to combine references need not be the subject of the instant invention. Second, it is respectfully pointed out that Bannerjee is relied upon to teach the conventionality of adding tonicity agents to pharmaceutical formulations.

Applicant argues, "There is no desirability provided by the references, i.e., no motivation, for one of ordinary skill in the art to adjust the tonicity of the Miller compositions by applying the method of Bannerjee. The only suggestion for such combination comes from the desire to support the rejection by picking out disclosures of the references to meet applicants' claims". This argument is not persuasive. As pointed out in the previous Office Action, one of skill would be motivated to add the tonicity adjusting agent of Bannerjee into the composition of Miller because of the expectation of achieving a product wherein the tonicity can be adjusted, wherein such an adjustment is beneficial since the tonicity can be adjusted to the individual needs of patients. Further, it is respectfully pointed out that every composition has tonicity.

Applicant argues, "There is no suggestion from Miller that there is any need or desire to adjust the tonicity of the Miller compositions. . .Further, there is no suggestion from Bannerjee or from Miller to suggest that a means for adjusting tonicity in a composition for effecting bronchodilating activity would be desired or even useful in a composition, such as Miller's, containing a radiopharmaceutical". This argument is not persuasive. It is respectfully pointed out that Bannerjee is relied upon to teach the conventionality of adding tonicity adjusting agents to pharmaceutical formulations, wherein the radiopharmaceutical of Miller is a pharmaceutical formulations. It is further respectfully pointed out that adjusting tonicity is beneficial, as in

administering a pharmaceutical formulation, it is most desirous to keep the body chemistry, i.e., electrolyte concentrations, as constant as possible for the well-being of the patient.

Applicant argues, "The previous Advisory Action alleged that, merely because the Miller, Blum and Bannerjee references all directed to pharmaceutical compositions administered in vivo in saline solution, it would be obvious to combine teachings of one reference with another". This argument is not persuasive, as Applicant has misconstrued the Examiner's statement. The instant rejection provides motivation to combine the reference, and in response to Applicant's previous arguments, the Examiner was stating that the three references were analogous, as they were all directed to pharmaceutical formulations that are administered in vivo.

Applicant argues, "There is no desirability indicated in the references, i.e., no motivation, for why one of ordinary skill in the art would want to adjust the tonicity of the Miller compositions by applying the method of Bannerjee". This argument is not persuasive, and has been addressed above and in the instant rejection.

Applicant argues, "Applicants do not understand the statement in the Office Action that the 'rejection does not apply the method of Bannerjee.' If the tonicity adjusting method of Bannerjee is not applied, there is no teaching at all regarding use of an iodide. In order to apply the teaching in Bannerjee regarding use of an iodide, the reference must be considered as a whole". This argument is not persuasive. Again, Applicant has taken out of context and misconstrued the Examiner's response to Applicant's arguments. The Examiner was unclear what Applicant was referring to in the previous Office Action when he stated "by applying the method of Bannerjee". The Examiner's response was merely to point out that Bannerjee was relied upon for teaching tonicity adjusting agents. The reference was considered as a whole.

Applicant argues, "The Office Action further alleges that tonicity is a concern for all pharmaceutical compositions. That may or may not be true; there is no evidence on the record to support this allegation, though. To the contrary, Bannerjee teaches that tonicity agents are merely optional and 'may' be added. Thus, it is clear that they are not required or desired in all pharmaceutical saline compositions". This argument is not persuasive. The instant argument does not mean that there is no motivation to add the tonicity adjusting agents of Bannerjee into the formulations of Miller. It is respectfully pointed out that the test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art.

Applicant argues, "It is alleged in the Office Action that the stabilization of the radiopharmaceutical would result from the characteristic properties of the suggested combined compositions. But the advantage in radionuclide stabilization would only be achieved on out of 70 chance the iodide salt is selected from all the agents of Bannerjee. Thus, it is not an inherent property of the Bannerjee tonicity agents because stabilizing a pharmaceutical would not 'necessarily and inevitably' occur". This argument is not persuasive. The combined references teach the instant composition, and since a compound and its properties are inseparable, the iodide ions of the combined references and those of the instant composition have the same properties.

Applicant argues, "The Office Action alleges that this argument is not persuasive because the claims do not recite any amounts. This is not correct. The claims literally recite the above-quoted language". This argument is not persuasive. Again, Applicant has mischaracterized and misconstrued the Examiner's response to Applicant's arguments. In the previous response

Applicant stated , "such combination would not suggest the use of an iodide tonicity adjusting agent in an amount sufficient. . .". The instant claims do not recite an "amount sufficient". Thus, such an argument is NOT commensurate in scope with the instant claims.

Additionally, as pointed out in the previous Office Action, tonicity refers to the response of cells or tissues to the solutions in which they are immersed. If cells are placed in a hypertonic solution, net movement of water will be out of the cell, causing the cell to shrivel. If cells are placed in a hypotonic solution, net movement of water will be into the cell, causing the cell to swell or burst. Thus, one skilled in the art would add sufficient solute(s) to the composition so that the composition has the correct osmolarity so that it will have the desired tonicity with respect to the cells that are being exposed to the composition.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is 571-272-0634. The examiner can normally be reached on M&R (5:30-4).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

lqw

SREENI PADMANABHAN
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